

10/814,194
L/COOK 12/7/05

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(FILE 'HOME' ENTERED AT 16:21:50 ON 07 DEC 2005)

FILE 'STNGUIDE' ENTERED AT 16:21:54 ON 07 DEC 2005

FILE 'HOME' ENTERED AT 16:21:59 ON 07 DEC 2005

FILE 'BIOSIS, CAPLUS, EMBASE, MEDLINE, CANCERLIT, JAPIO' ENTERED AT
16:22:19 ON 07 DEC 2005

L1 61 S (ANTI PAF) AND ASSAY?
L2 35 S L1 AND PD<1999
L3 12 S L2 AND HUMAN?

=>

10/814,194
LYCOK 12/7/05

d his

(FILE 'HOME' ENTERED AT 09:53:28 ON 07 DEC 2005)

FILE 'BIOSIS, CAPLUS, EMBASE, MEDLINE, CANCERLIT, JAPIO' ENTERED AT
09:53:55 ON 07 DEC 2005

L1 617 S PAF AND PREGNANCY
L2 431 S (ANTI PAF)
L3 0 S L2 AND ABORTION?
L4 199 DUPLICATE REMOVE L2 (232 DUPLICATES REMOVED)
L5 149 S L4 AND PD<1999
L6 7 S L1 AND L2
L7 5 DUPLICATE REMOVE L6 (2 DUPLICATES REMOVED)

=>

d his

(FILE 'HOME' ENTERED AT 09:53:28 ON 07 DEC 2005)

FILE 'BIOSIS, CAPLUS, EMBASE, MEDLINE, CANCERLIT, JAPIO' ENTERED AT
09:53:55 ON 07 DEC 2005

L1	617 S PAF AND PREGNANCY
L2	431 S (ANTI PAF)
L3	0 S L2 AND ABORTION?
L4	199 DUPLICATE REMOVE L2 (232 DUPLICATES REMOVED)
L5	149 S L4 AND PD<1999
L6	7 S L1 AND L2
L7	5 DUPLICATE REMOVE L6 (2 DUPLICATES REMOVED)

=>

ANSWER 10 OF 149 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on
STN

AN 1996:227510 BIOSIS

DN PREV199698783639

TI Effect of platelet-activating factor (PAF) on preimplantation mouse
B-6D-2F-1/J embryo formation.

AU Roudebush, William E. [Reprint author]; Duralia, David R.; Butler, William
J.

CS Div. Reproductive Endocrinol., Dep. Obstetrics Gynecol., Med. Univ. South
Carolina, Charleston, SC 29425-2233, USA

SO American Journal of Reproductive Immunology, (1996) Vol. 35, No.

3, pp. 272-276.

ISSN: 1046-7408.

DT Article

LA English

ED Entered STN: 8 May 1996

Last Updated on STN: 8 May 1996

AB Platelet-activating factor (1-O-alkyl-2-acetyl-sn-glycero-3-phosphocholine;
PAF) is a potent signaling phospholipid that has been implicated in a
variety of reproductive processes. Human, rabbit, and mouse
preimplantation embryos produce and secrete PAF. **Anti-
PAF** antibodies interfere with mouse preimplantation development.
A controversy exists on whether exogenous PAF is beneficial to
preimplantation embryo development. The study objective was to determine
the effect of exogenous PAF on embryo formation. One-cell mouse
B-6D-2F-1/J embryos were collected from PMSG/hCG primed females mated with
fertile males. Embryos were exposed to PAF (0-10 mu-M) in MEM (0.3% BSA)
for 15 min, then cultured in MEM (0.3% BSA) in a 5% CO-2 in air, 95%
relative humidity at 37 degree C atmosphere, for 120 hr to the hatched
blastocyst stage. PAF (0.1 or 0.01 mu-M) significantly (P lt 0.05)
improved preimplantation embryo development and formation in vitro. PAF
at higher doses had no significant effect. Supplementation of culture
medium with exogenous PAF was beneficial to preimplantation embryo
development in B-6D-2F-1/J mice.

CC Cytology - Animal 02506

Biochemistry studies - Proteins, peptides and amino acids 10064

Biochemistry studies - Lipids 10066

Reproductive system - Physiology and biochemistry 16504

Endocrine - General 17002

Development and Embryology - Experimental 25504

IT Major Concepts

Cell Biology; Development; Endocrine System (Chemical Coordination and
Homeostasis); Reproductive System (Reproduction)

IT Miscellaneous Descriptors

SIGNALING PHOSPHOLIPID

ORGN Classifier

Muridae 86375

Super Taxa

Rodentia; Mammalia; Vertebrata; Chordata; Animalia

Organism Name

Muridae

Taxa Notes

Animals, Chordates, Mammals, Nonhuman Vertebrates, Nonhuman Mammals,
Rodents, Vertebrates

AN 1989:70050 CAPLUS
 DN 110:70050
 ED Entered STN: 04 Mar 1989
 TI Compositions and methods for fertility control using platelet-activating factor, its analogs and antagonists
 IN O'Neill, Christopher
 PA Royal North Shore Hospital, Australia
 SO Eur. Pat. Appl., 13 pp.
 CODEN: EPXXDW
 DT Patent
 LA English
 IC ICM A61K031-685
 ICS A61K031-55; A61K031-557; A61K037-64; A61K031-47; A61K031-20; A61K031-34; A61K031-565; A61K037-02
 CC 2-3 (Mammalian Hormones)
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 261798	A2	19880330	EP 1987-307439	19870821
	EP 261798	A3	19900509		
	R: AT, BE, CH, DE, FR, GB, GR, IT, LI, LU, NL, SE				
	AU 8777189	A1	19880225	AU 1987-77189	19860822
	AU 608530	B2	19910411		
	US 4879285	A	19891107	US 1987-86900	19870818
	DK 8704315	A	19880223	DK 1987-4315	19870819
	ZA 8706215	A	19880427	ZA 1987-6215	19870821
	JP 63115819	A2	19880520	JP 1987-209119	19870822
PRAI	AU 1986-7642	A	19860822		

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
EP 261798	ICM	A61K031-685
	ICS	A61K031-55; A61K031-557; A61K037-64; A61K031-47; A61K031-20; A61K031-34; A61K031-565; A61K037-02
US 4879285	NCL	514/075.000; 514/120.000; 514/841.000; 514/843.000

OS MARPAT 110:70050

AB The in vivo or in vitro administration of platelet-activating factor [sn-R2OCH2CH(O2CR1)CH2OP(:O)(O-)OCH2CH2N+R33 (I; R1 = R3 = Me; R2 = C16 or C18 alkyl)] (PAF) or PAF analogs (I; R1 = C1-6 alkyl; R2 = C10-24 alkyl; R3 = C1-3 alkyl) enhances the viability of fertilized embryos and improves rates of implantation in the uterus. Conversely, reduction of PAF concentration by in vivo administration of PAF antagonists such as iloprost or anti-PAF antibodies has a contraceptive effect, particularly when used in conjunction with a postcoital contraceptive such as estrogen or a prostaglandin. Ovulation-synchronized mice were mated and iloprost (PAF antagonist) was administered at 1.0 or 2.0 µg/30 g body weight i.p. 6 times on days 1-4 of pregnancy. The implantation rate was decreased from about 75% in controls to 40-50% by this treatment. In contrast, when 2-cell embryos collected from superovulated mated mice were cultured to the blastocyst stage in human tubal fluid medium containing bovine serum albumin and PAF (0.1 µg/mL) and transferred to pseudopregnant females on day 3 of pseudopregnancy, the implantation rate was increased from 34.3 (control) to 58.6%.

ST fertility control platelet activating factor; contraceptive iloprost; embryo implantation platelet activating factor

IT Fertility
 (blood platelet-activating factor and antagonists effect on)

IT Contraceptives
 (blood platelet-activating factor antagonists)

IT Uterus
 (embryo implantation in, blood platelet-activating factor and antagonists effect on)

IT Embryo
 (implantation of, blood platelet-activating factor and antagonists
 effect on)

IT Corpus luteum
 (progesterone secretion by, blood platelet-activating factor effect on)

IT Antibodies
 RL: BIOL (Biological study)
 (to blood platelet-activating factor, as contraceptives)

IT 15291-77-7, BN 52021 28981-97-7, Alprazolam 78919-13-8, Iloprost
 95851-37-9, Kadsurenone 99103-35-2, L 652731 104786-62-1, SRI 63441
 109516-82-7, SRI 63675 118817-52-0, SRI 64412 118817-53-1, SRI 64557
 RL: BIOL (Biological study)
 (as contraceptive)

IT 65154-06-5, Blood platelet-activating factor
 RL: BIOL (Biological study)
 (fertility control with)

IT 57-83-0, Progesterone, biological studies
 RL: BIOL (Biological study)
 (secretion of, by corpus luteum, blood platelet-activating factor
 effect on)

IT Embryo
 (implantation of, blood platelet-activating factor and antagonists
 effect on)

IT Corpus luteum
 (progesterone secretion by, blood platelet-activating factor effect on)

IT Antibodies
 RL: BIOL (Biological study)
 (to blood platelet-activating factor, as contraceptives)

IT 15291-77-7, BN 52021 28981-97-7, Alprazolam 78919-13-8, Iloprost
 95851-37-9, Kadsurenone 99103-35-2, L 652731 104786-62-1, SRI 63441
 109516-82-7, SRI 63675 118817-52-0, SRI 64412 118817-53-1, SRI 64557
 RL: BIOL (Biological study)
 (as contraceptive)

IT 65154-06-5, Blood platelet-activating factor
 RL: BIOL (Biological study)
 (fertility control with)

IT 57-83-0, Progesterone, biological studies
 RL: BIOL (Biological study)
 (secretion of, by corpus luteum, blood platelet-activating factor
 effect on)

ANSWER 4 OF 5 MEDLINE on STN

AN 95329913 MEDLINE

DN PubMed ID: 7606155

TI Anti-platelet activating factor (PAF) antibody inhibits CFW mouse preimplantation embryo development.

AU Roudebush W E; Mathur S; Butler W J

CS Department of Obstetrics and Gynecology, Medical University of South Carolina, Charleston 29425-2233, USA.

SO Journal of assisted reproduction and genetics, (1994 Sep) 11 (8) 414-8. Journal code: 9206495. ISSN: 1058-0468.

CY United States

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Priority Journals

EM 199508

ED Entered STN: 19950828
Last Updated on STN: 19950828
Entered Medline: 19950814

AB OBJECTIVE: Our purpose was to investigate the effect of **anti-PAF** antibodies on CFW mouse embryo development in vitro. DESIGN: We studied the in vitro development of CFW mouse one-cell-stage embryos cultured in MEM supplemented with **anti-PAF**, anti-IgG, or MEM alone to the hatched blastocyst stage. RESULTS: Mouse embryos cultured with **anti-PAF** (1:5 dilution; 61%) significantly decreased embryo development compared to controls (MEM alone; 93%), whereas embryos cultured in anti-mouse IgG-supplemented MEM (1:10 dilution; 93%) had no effect. CONCLUSIONS: The results provide additional evidence that **PAF** is produced and secreted by cleavage-stage embryos and is required during the preimplantation period.

CT Check Tags: Female; Male
Animals
Antibodies: IM, immunology
*Antibodies: PD, pharmacology
Blastocyst: DE, drug effects
Blastocyst: IM, immunology
Blastocyst: PH, physiology
Cells, Cultured
*Embryonic Development: IM, immunology
*Embryonic and Fetal Development: IM, immunology
Horses
Humans
Immunoglobulin G: IM, immunology
Mice
Mice, Inbred Strains
*Platelet Activating Factor: IM, immunology
Platelet Activating Factor: ME, metabolism
Platelet Activating Factor: PD, pharmacology
Pregnancy
Sheep

CN 0 (Antibodies); 0 (Immunoglobulin G); 0 (Platelet Activating Factor)

ANSWER 4 OF 5 MEDLINE on STN

AN 95329913 MEDLINE

DN PubMed ID: 7606155

TI Anti-platelet activating factor (PAF) antibody inhibits CFW mouse preimplantation embryo development.

AU Roudebush W E; Mathur S; Butler W J

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CY United States

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Priority Journals

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ED Entered STN: 19950828
Last Updated on STN: 19950828
Entered Medline: 19950814

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Antibodies: IM, immunology
*Antibodies: PD, pharmacology
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Blastocyst: IM, immunology
Blastocyst: PH, physiology
Cells, Cultured
*Embryonic Development: IM, immunology
*Embryonic and Fetal Development: IM, immunology
Horses
Humans
Immunoglobulin G: IM, immunology
Mice
Mice, Inbred Strains
*Platelet Activating Factor: IM, immunology
Platelet Activating Factor: ME, metabolism
Platelet Activating Factor: PD, pharmacology
Pregnancy
Sheep

CN 0 (Antibodies); 0 (Immunoglobulin G); 0 (Platelet Activating Factor)

DUPLICATE 1

AN 2001:370034 BIOSIS

DN PREV200100370034

TI Fluorometric detection of platelet activating factor receptor in cultured oviductal epithelial and stromal cells and endometrial stromal cells from bovine at different stages of the oestrous cycle and early **pregnancy**.

AU Tiemann, U. [Reprint author]; Viergutz, T.; Jonas, L.; Wollenhaupt, K.; Poehland, R.; Kanitz, W.

CS Unit of Reproductive Biology, Research Institute for the Biology of Farm Animals, 18196, Dummerstorf, Germany
tiemann@fhn-dummerstorf.de

SO Domestic Animal Endocrinology, (April, 2001) Vol. 20, No. 3, pp. 149-164. print.

CODEN: DANEEE. ISSN: 0739-7240.

DT Article

LA English

ED Entered STN: 8 Aug 2001

Last Updated on STN: 19 Feb 2002

AB During the oestrous cycle and early **pregnancy**, the oviduct and uterus undergo a variety of morphological and physiological modifications in which the platelet activating factor receptor (**PAF-R**) plays an important role. **PAF-R** levels were quantified in bovine oviductal epithelial and stromal cells and endometrial stromal cells at days 2 to 4, 12, and 20 of the estrous cycle and during early **pregnancy**. Cells were grown in vitro and their intracellular **PAF-R** concentration was measured by flow cytometry using a polyclonal **anti-PAF-R** antibody system. A significant increase ($P<0.05$) in the portion of **PAF-R**-positive oviductal epithelial and stromal cells was detected in both non-pregnant and pregnant cattle on days 2 to 4 in comparison to day 12 and 20. In endometrial stromal cells derived from day 20 pregnant bovine, a significant increase ($P<0.05$) in **PAF-R** staining was observed in comparison to the day 20 non-pregnant and days 2 to 4 or 12 pregnant and non-pregnant animals. The **PAF-R** was detected in oviductal cells by using immunoblotting and immuno-gold postembedding method. Positive binding of the **anti-PAF-R** antibody was found on the cell membrane and in the cytoplasm. We concluded that the increased **PAF-R** concentration measured in cultured oviductal epithelial and stromal cells of cyclic and pregnant heifers on days 2 to 4 was hormonally regulated. The increased **PAF-R** in endometrial stromal cells on day 20 of pregnant heifers was a **pregnancy**-specific effect and may mediate a local increase in endometrial vascular permeability known to precede the implantation.

CC Cytology - Animal 02506

Biochemistry studies - General 10060

Reproductive system - Physiology and biochemistry 16504

Animal production - General and methods 26502

Animal production - Breeds and breeding 26506

Immunology - General and methods 34502

IT Major Concepts

Animal Husbandry (Agriculture); Biochemistry and Molecular Biophysics; Reproductive System (Reproduction)

IT Parts, Structures, & Systems of Organisms

cell membrane; cytoplasm; endometrial stromal cells: reproductive system, cultured; oviduct: reproductive system; oviductal epithelial cell: reproductive system, cultured; oviductal stromal cells: reproductive system, cultured; uterus: reproductive system

IT Chemicals & Biochemicals

anti-platelet activating factor receptor [**anti-PAF-R**]: antibody; platelet activating factor receptor [**PAF-R**]

IT Methods & Equipment

flow cytometry: cytophotometry: CB, measurement method; fluorometry:

ANSWER 1 OF 5 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
DUPLICATE 1

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DN PREV200100370034

TI Fluorometric detection of platelet activating factor receptor in cultured oviductal epithelial and stromal cells and endometrial stromal cells from bovine at different stages of the oestrous cycle and early pregnancy.

AU Tiemann, U. [Reprint author]; Viergutz, T.; Jonas, L.; Wollenhaupt, K.; Poehland, R.; Kanitz, W.

CS Unit of Reproductive Biology, Research Institute for the Biology of Farm Animals, 18196, Dummerstorf, Germany
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CC Cytology - Animal 02506

Biochemistry studies - General 10060

Reproductive system - Physiology and biochemistry 16504

Animal production - General and methods 26502

Animal production - Breeds and breeding 26506

Immunology - General and methods 34502

IT Major Concepts

Animal Husbandry (Agriculture); Biochemistry and Molecular Biophysics;

Reproductive System (Reproduction)

IT Parts, Structures, & Systems of Organisms

cell membrane; cytoplasm; endometrial stromal cells: reproductive system, cultured; oviduct: reproductive system; oviductal epithelial cell: reproductive system, cultured; oviductal stromal cells: reproductive system, cultured; uterus: reproductive system

IT Chemicals & Biochemicals

anti-platelet activating factor receptor [anti-PAF-R]: antibody; platelet activating factor receptor [PAF-R]

IT Methods & Equipment

flow cytometry; cytophotometry; CB, measurement method; fluorometry:

detection method, photometry: CB; immuno-gold postembedding method:
detection method; immunoblotting: detection method

IT Miscellaneous Descriptors

estrous cycle stages; **pregnancy**

ORGN Classifier

Bovidae 85715

Super Taxa

Artiodactyla; Mammalia; Vertebrata; Chordata; Animalia

Organism Name

bovine: female, heifer

Taxa Notes

Animals, Artiodactyls, Chordates, Mammals, Nonhuman Vertebrates,
Nonhuman Mammals, Vertebrates

detection method, photometry: CB; immuno-gold postembedding method:
detection method; immunoblotting: detection method

IT Miscellaneous Descriptors

estrous cycle stages; **pregnancy**

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Artiodactyla; Mammalia; Vertebrata; Chordata; Animalia

Organism Name

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Taxa Notes

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Nonhuman Mammals, Vertebrates

AN 1989:70050 CAPLUS
 DN 110:70050
 ED Entered STN: 04 Mar 1989
 TI Compositions and methods for fertility control using platelet-activating factor, its analogs and antagonists
 IN O'Neill, Christopher
 PA Royal North Shore Hospital, Australia
 SO Eur. Pat. Appl., 13 pp.
 CODEN: EPXXDW
 DT Patent
 LA English
 IC ICM A61K031-685
 ICS A61K031-55; A61K031-557; A61K037-64; A61K031-47; A61K031-20; A61K031-34; A61K031-565; A61K037-02
 CC 2-3 (Mammalian Hormones)
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 261798	A2	19880330	EP 1987-307439	19870821
	EP 261798	A3	19900509		
	R: AT, BE, CH, DE, FR, GB, GR, IT, LI, LU, NL, SE				
	AU 8777189	A1	19880225	AU 1987-77189	19860822
	AU 608530	B2	19910411		
	US 4879285	A	19891107	US 1987-86900	19870818
	DK 8704315	A	19880223	DK 1987-4315	19870819
	ZA 8706215	A	19880427	ZA 1987-6215	19870821
	JP 63115819	A2	19880520	JP 1987-209119	19870822
PRAI	AU 1986-7642	A	19860822		

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
EP 261798	ICM	A61K031-685
	ICS	A61K031-55; A61K031-557; A61K037-64; A61K031-47; A61K031-20; A61K031-34; A61K031-565; A61K037-02
US 4879285	NCL	514/075.000; 514/120.000; 514/841.000; 514/843.000

OS MARPAT 110:70050

AB The in vivo or in vitro administration of platelet-activating factor [sn-R2OCH2CH(O2CR1)CH2OP(:O)(O-)OCH2CH2N+R33 (I; R1 = R3 = Me; R2 = C16 or C18 alkyl)] (PAF) or PAF analogs (I; R1 = C1-6 alkyl; R2 = C10-24 alkyl; R3 = C1-3 alkyl) enhances the viability of fertilized embryos and improves rates of implantation in the uterus. Conversely, reduction of PAF concentration by in vivo administration of PAF antagonists such as iloprost or anti-PAF antibodies has a contraceptive effect, particularly when used in conjunction with a postcoital contraceptive such as estrogen or a prostaglandin. Ovulation-synchronized mice were mated and iloprost (PAF antagonist) was administered at 1.0 or 2.0 µg/30 g body weight i.p. 6 times on days 1-4 of pregnancy. The implantation rate was decreased from about 75% in controls to 40-50% by this treatment. In contrast, when 2-cell embryos collected from superovulated mated mice were cultured to the blastocyst stage in human tubal fluid medium containing bovine serum albumin and PAF (0.1 µg/mL) and transferred to pseudopregnant females on day 3 of pseudopregnancy, the implantation rate was increased from 34.3 (control) to 58.6%.

ST fertility control platelet activating factor; contraceptive iloprost; embryo implantation platelet activating factor

IT Fertility
 (blood platelet-activating factor and antagonists effect on)

IT Contraceptives
 (blood platelet-activating factor antagonists)

IT Uterus
 (embryo implantation in, blood platelet-activating factor and antagonists effect on)

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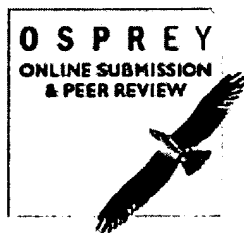
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Platelet-activating factor-antagonists reduce implantation in mice at low doses only

C O'Neill

Abstract

The effects of a number of platelet-activating factor (PAF)-antagonists on embryo implantation were investigated. Mice were treated from Day 1 to Day 4 of pregnancy with three defined PAF-antagonists: SRI 63 441, BN 52021, and WEB 2086. Necroscopies were performed on Day 8 and the number of implantation sites, the implantation rate (number of implanted embryos compared with the number of corpora lutea) and the proportion of animals pregnant were determined. Each agent caused a reduction in the number of implantation sites at relatively low doses. The dose that had a maximum contragestational effect was 40 micrograms, 10 micrograms and 10 micrograms (per 30 g bodyweight per day) for SRI 63 441, WEB 2086 and BN 52021 respectively. This contragestational effect was completely lost at twice (SRI 63 441), five times (WEB 2086) and ten times (BN 52021) the most effective dose. Treatment with WEB 2086 on the day of implantation (Day 4) by intraperitoneal injection or instillation into the uterus only did not significantly reduce the implantation rate and neither did treatment after implantation (Days 5-8). The results show that the pharmacology of PAF-antagonists in early pregnancy is not simple. An understanding of the actions of these agents in early pregnancy will require a detailed knowledge of their pharmacokinetics, pharmacodynamics and targets of action in early pregnancy.

Reproduction, Fertility and Development 7(1) 51 - 57

Full text doi:10.1071/RD9950051

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